Complete Summary

GUIDELINE TITLE

Management of type 2 diabetes mellitus.

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Management of type 2 diabetes mellitus. Ann Arbor (MI): University of Michigan Health System; 2004 Jul. 18 p. [4 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Management of diabetes mellitus. Guidelines for clinical care. Ann Arbor (MI): University of Michigan Health System; 1998. 12 p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Type 2 diabetes mellitus

GUIDELINE CATEGORY

Diagnosis
Management
Prevention
Screening
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Geriatrics
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To improve adherence to important, morbidity-reducing recommendations for preventing, detecting, and managing diabetic complications

TARGET POPULATION

Adults seen in primary care settings including those at risk for or diagnosed with diabetes mellitus

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Fasting glucose
2. Oral glucose tolerance test (OGTT)
3. HbA1c

Screening/Prevention/Treatment/Management

1. Screening, prevention, and treatment of complications associated with diabetes, addressing considerations in the following areas:
    - Cardiovascular disease
        - Screening for hypertension, hyperlipidemia, and smoking
        - Smoking cessation programs and alternative nicotine delivery systems or pharmacologic therapies
        - Aspirin therapy for cardiovascular protection
        - Hypertension: thiazide diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARBs), beta-blockers, calcium channel blockers, and $alpha_1$-adrenergic receptor blockers
        - Lipid screening and treatment (statins)
    - Microvascular complications (retinopathy, nephropathy, neuropathy)
        - Dilated retinal examinations
        - Screening for microalbuminuria: spot urinary albumin-creatinine ratio
        - ACE inhibitors, ARBs, and other antihypertensives to reduce the rate of progression to overt proteinuria

        - Diabetic foot examination and care; treatment of diabetic foot ulcers; monofilament testing of feet
        - Treatment of painful neuropathy with nonsteroidal anti-inflammatory drugs (NSAIDs), tricyclic antidepressants, anti-seizure medications, other pharmacologic agents and acupuncture.
2. Glycemic management
    - Oral agents
        - Metformin
        - Sulfonylureas
        - Thiazolidinediones
        - Alpha-glucosidase inhibitors
        - Non-sulfonylurea insulin secretagogues
        - Combination oral therapy
    - Combination oral/insulin therapy
        - Insulin agents
            - Rapid-acting: lispro (Humalog), aspart (NovoLog)
            - Short acting (Regular)
            - Intermediate-acting (NPH, Lente, Ultra Lente)
            - Long-acting: glargine (Lantus)
            - Intermediate and short-acting mixtures: NPL/Humalog (Humalog Mix 75/25 & 50/50), NPH/NovoLog (NovoLog Mix 70/30), NPH/Reg (Humulin 70/30 and Novolin 70/30).
3. Glycemic monitoring, including self-monitoring of blood glucose and HbA_{1c} measurement
4. Diabetes self-management education (DSME)
5. Preconception counseling and pregnancy
6. Complementary and alternative therapies
7. Consultation or referral for special circumstances

MAJOR OUTCOMES CONSIDERED

- Progression from impaired glucose tolerance (IGT) to diabetes
- Glycemic control, based on percent hemoglobin A1c or glycosylated hemoglobin
- Incidence of cardiovascular and microvascular disease (including retinopathy, nephropathy, and neuropathy)
- Incidence of end-stage outcomes of diabetes including blindness, renal failure, and amputation
- Mortality rate among patient with diabetes
- Cost of medical care
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature search for this update began with the results of the literature searches performed for the previous updates of this guideline. When recent evidence reviews were not available for a topic, new searches of primary literature were performed. For these topics literature searches were conducted on Medline in February 2003. The searches were performed prospectively using the major key words of diabetes mellitus; consensus development conferences, practice guidelines, guidelines, outcomes and process assessment (health care); clinical trials, controlled clinical trials, multicenter studies; English language; and published from 1995 to present. Terms for specific topic searches within the major key words included: alpha-glucosidase inhibitors, thiazolidinediones, nonsulfonyluric secretagogues (repaglinide, nateglinide), new insulins (glargine, aspart, lispro); chromium, nephropathy (screening, treatment), and neuropathy (screening and treatment).

The search was conducted in components each keyed to a specific causal link in a formal problem structure. The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was single cycle.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of evidence for the most significant recommendations:

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Consideration of benefits, harms, costs, and patient preferences.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The guideline developer reviewed cost analyses.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

University of Michigan Health System (UMHS) guidelines are reviewed by leadership in departments to which the content is most relevant. This guideline concerning depression was reviewed by members of the following departments: Endocrinology; Family Medicine; General Medicine; Obstetrics and Gynecology. Guidelines are approved by the Primary Care Executive Committee (PCEC) and the Executive Committee of Clinical Affairs (ECCA).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): The following key points summarize the content of the guideline. Refer to the full text for additional information, including dosing and cost considerations for oral agents for the management of type 2 diabetes and self-management topics. The levels of evidence [A–D] are defined at the end of the "Major Recommendations" field.

Screening

Consider screening for diabetes beginning at age 45 at 3–year intervals, particularly if body mass index (BMI) $\geq$25 kg/m^2. However, little evidence is presently available on screening for diabetes [evidence: D].

Prevention

In individuals at risk for diabetes (see Table 1 in original guideline document), diet, exercise, and pharmacologic interventions can delay or prevent type 2 diabetes [A].

Diagnosis

Either two separate fasting glucoses ≥126 mg/dL, or if symptoms, a glucose ≥200 mg/dL confirmed on a separate day by a fasting glucose ≥126 mg/dL [B]. (See Table 1 in the original guideline document.)

Treatment

Diet, exercise, and pharmacologic interventions should be initiated for:

- Glycemic control [A] University of Michigan Health System (UMHS) preferred agents are metformin, glipizide, and pioglitazone (Actos®)
- Lipid control [A]
- Hypertension control [A]
- Cardiovascular risk reduction [A]

Ongoing Screening and Management

Routine screening and prevention efforts for cardiovascular risk factors (hypertension, hyperlipidemia, tobacco use) and for microvascular disease (retinopathy, nephropathy, neuropathy) are recommended to be performed in the following time frames. (See the original guideline document for management of risk factors, complications, and glycemia.)

Each regular diabetes visit	Every 3 to 6 months	Annually (see Table 2 in the original guideline document)
• Diabetes visit every 3 months for patients on insulin; every 6 months for patients on oral agents or diet only [D] • Weight checked [D] • Blood pressure measured and controlled [A] (see Table 2 in the original guideline document) • Inspect feet each visit and areas of concern discussed [A] (see Table 2 in the original guideline document)	• HbA1c and glycemic control optimized [A] (see Table 3 in the original guideline document)	• Dilated retinal examination by an eye care specialist [B] and treatment of retinopathy [A] (Biannually if low risk, see Table 2 in the original guideline document) • Urine protein and, if normal, screen for microalbuminuria [B] Angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor antagonists (ARBs) for micro-albuminuria or proteinuria [A] • Monofilament testing of feet [A] • Lipids measured [B] and treated [A] • Smoking status assessed • Other important self-management actions reviewed and reinforced (see Table 4 in the original

Each regular diabetes visit	Every 3 to 6 months	Annually (see Table 2 in the original guideline document)
• Smoking cessation counseling provided for patients with tobacco dependence [B] (see Table 2 in the original guideline document) • Very important self-management actions reviewed and reinforced [A] (see Table 4 in the original guideline document)		guideline document)

Special considerations: Pregnancy. Preconception counseling and glycemic control in women with diabetes mellitus results in optimal maternal and fetal outcomes [B].

Definitions:

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is identified and graded for the most significant recommendations (see "Major Recommendations").

Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data. If randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved prevention, detection and management of diabetic complications
- Reduced morbidity from type 2 diabetes mellitus

Subgroups Most Likely to Benefit:

- Screening: The American Diabetes Association (ADA) suggests screening be considered earlier or at more frequent intervals in those with risk factors including family history, physical inactivity, minority ethnicity, previously identified impaired fasting glucose or impaired glucose tolerance, a history of gestational diabetes, hypertension, high-density lipoprotein (HDL) cholesterol $\leq$35 mg/dL and/or a triglyceride level of $\geq$250 mg/dL, polycystic ovarian disease, or a history of vascular disease.
- Minorities: Minorities have a prevalence of Type 2 diabetes mellitus that is 2 to 6 times greater than that of Caucasians. The morbidity and mortality rates are higher for minorities than for Caucasians, and the rate is increasing. More aggressive management of diabetes in minority populations may be indicated.

POTENTIAL HARMS

- Risk of tight control: The major risk of intensive glycemic control is hypoglycemia.
- Side effects of antihypertensive agents:
    - High-dose thiazide diuretics have been reported to have a variety of adverse effects including worsening of hyperlipidemia, deterioration of glycemic control, impotence, and increased mortality, so thiazides should be used in low doses.
    - Angiotensin-converting enzyme (ACE) inhibitors can lead to cough; ACE inhibitors and angiotensin II receptor antagonists (ARBs) can lead to renal insufficiency, and hyperkalemia; careful monitoring of serum electrolytes is therefore warranted with these agents.
    - Beta-blockers were more frequently discontinued and led to more weight gain and higher doses of glucose-lowering agents than ACE inhibitors. If a beta-blocker is used, it should be cardioselective.
    - Alpha$_1$-adrenergic receptor blockers do not have adverse glycemic or lipid effects but may aggravate postural hypotension in some persons with diabetes.
- Side effects of drug therapy for hyperlipidemia:
    - The use of nicotinic acid for hypertriglyceridemia should be used with caution because it may worsen hyperglycemia.
    - For primary prevention, younger patients who are otherwise at lower risk may receive less benefit from lipid lowering statins.

- Side effects of oral hypoglycemic agents:
    - Gastrointestinal side effects, including diarrhea, are seen in up to 30% of patients using metformin.
    - Gastrointestinal side effects including pain, flatulence, and diarrhea are common with alpha-glucosidase inhibitors; although these effects usually diminish over time (4–8 weeks), they frequently lead to discontinuation of the drug.
    - Rosiglitazone has been associated with 2 case reports of hepatotoxicity; however, the relationships may not have been causal and liver function tests returned to normal when the drug was discontinued.

Subgroups Most Likely to be Harmed:

Individuals with the following characteristics are at heightened risk with tight glycemic control:

- History of severe hypoglycemia (inability to treat without assistance): any episodes within the past year and/or more than 2 episodes ever
- Hypoglycemia unawareness
- Advanced cardiovascular or cerebrovascular disease
- Autonomic neuropathy (especially cardiac)
- Comorbidities / medications that impair the detection of hypoglycemia (e.g., beta-blockers, CNS-acting drugs, alteration in mental status)
- Lack of mobility or lives alone

CONTRAINDICATIONS

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Some members of the dihydropteridine class of calcium channel blockers may increase urinary albumin excretion and should be avoided in patients with microalbuminuria.

QUALIFYING STATEMENTS

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Management of type 2 diabetes mellitus. Ann Arbor (MI): University of Michigan Health System; 2004 Jul. 18 p. [4 references]

ADAPTATION

This guideline was partially adapted as follows:

- Screening and glycemic goal recommendations were based on "American Diabetes Association. Clinical practice recommendations 2004. Diabetes Care. 2004;27(Suppl 1):S1–S140."
- Screening and treatment of hypertension and lipid levels in type 2 diabetes recommendations are based on "Lipid control in the management of type 2 diabetes mellitus: A Clinical Practice Guideline from the American College of Physicians, Clinical Efficacy Assessment Subcommittee (2004)."

DATE RELEASED

1996 May (revised 2004 Jul)

GUIDELINE DEVELOPER(S)

University of Michigan Health System - Academic Institution

SOURCE(S) OF FUNDING

Internal funding for UMHS guidelines is provided by the Office of Clinical Affairs. No external funds are used.

GUIDELINE COMMITTEE

Diabetes Mellitus Guideline Team

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

Team Member/Relationship/Company

Martha Funnell, MS, RN (Consultant: Aventis, Pfizer, Novo Nordisk, Takeda)
Van Harrison, PhD (None)
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GUIDELINE AVAILABILITY

Electronic copies: Available for download in Portable Document Format (PDF) from the University of Michigan Health System Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following are available:

- Type 2 (non-insulin-dependent) diabetes mellitus. Patient education handout. University of Michigan Health System; 2004 Apr. Various p.

Electronic copies: Available from the University of Michigan Health System Web site.

- Blood glucose monitoring. Patient education handout. University of Michigan Health System; 2004 Apr. Various p.

Electronic copies: Available from the University of Michigan Health System Web site.

- Hypoglycemia (insulin reaction). Patient education handout. University of Michigan Health System; 2004 Apr. Various p.

Electronic copies: Available from the University of Michigan Health System Web site.

- Diabetes and exercise. Patient education handout. University of Michigan Health System; 2004 Apr. Various p.

Electronic copies: Available from the University of Michigan Health System Web site.

- Long term complications of diabetes. Patient education handout. University of Michigan Health System; 2004 Apr. Various p.

Electronic copies: Available from the University of Michigan Health System Web site.

NGC STATUS

This summary was completed by ECRI on May 20, 1999. The information was verified by the guideline developer on June 17, 1999. This NGC summary was updated by ECRI on October 12, 2004. The updated information was verified by the guideline developer on October 22, 2004.

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